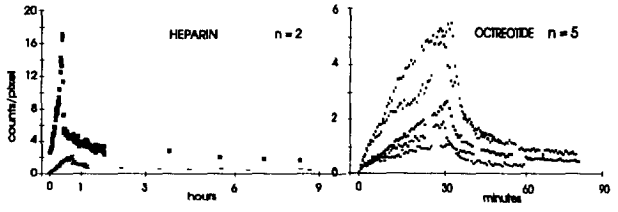
accumulation was observed for Tc-99m *H* and In-111 *O* (linear fitting: *H:* r = 0.97 ± 0.02; *O:* r = 0.98 ± 0.02) followed at infusion stop by a biexponential washout (biexponential fitting: *H:* r = 0.96 ± 0.02; *O:* r = 0.98 ± 0.02). Local retention time, defined as 5 concentration half-lives and derived from the 2nd slow washout phase, thought to reflect tissular washout, was for H 18 ± 2 h and for *O* 7 ± 3 h. Of the totally infused dose for *H* 6.8% and 0.5% (123 and 11 IU; 644 and 58 μg) and for *O* 0.3% ± 0.2% (0.55 ± 0.37 ng) remained at the site of delivery.



In conclusion administration of radiolabelled drugs allows to assess local pharmacokinetics and to quantify local drug retention-time and local retained amount of drug.

9:00

772-3 Heparin Delivery at the Site of Angioplasty with a Novel Drug Delivery Sleeve: Initial Clinical Series

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The LocalMed InfusaSleeve (IS) is a multi-lumen array with distal micro perforations designed to deliver agent at the site of angioplasty. Prior to the procedure, the IS is loaded onto a standard dilatation catheter (DC). Using standard technique, angioplasty is performed with the IS retracted. After lesion dilatation, the IS is tracked over the DC, aligning the micro perforation region of the IS with the balloon. The balloon is reinflated bringing the array into close proximity to the arterial wall. Agent(s) is delivered at specific pressures independent of balloon inflation. We have previously shown that agent delivery into the wall is dependent upon balloon inflation and drug delivery pressures. A pilot series was performed to evaluate the safety of heparin delivery via the IS.

A total of 21 patients [emergent/urgent (2), elective cases (19)] with lesions at a variety of anatomic sites [LAD(10), LCx(3), ramus intermedius(1), RCA(6) and vein graft (1)] and complexity [ACC/AHA Lesion Type: A(8), B1(10), B2(3)] were attempted. Following PTCA, heparin (1,000 U/ml) was delivered via the IS into the arterial lumen (balloon inflation pressure = 0.5 atm, drug delivery pressure = 40 psi). Failure to track the IS was noted in 2 cases. In 2 cases (RCA) a dissection was noted following agent infusion [NHLBI Type: A(1), B(1)]. The IS was used in conjunction with standard guide catheters [8 fr (15), 9 fr (6)], DC and guide wires. At discharge, no complications were noted.

We Conclude: 1) The IS can be used safely at a variety of anatomic sites, 2) The IS is compatible with standard PTCA equipment. 3) Local delivery of agent via LocalMed InfusaSleeve is a promising approach to reduce abrupt closure and restenosis.

9:15

772-4 Intravascular Heating Facilitates Local Heparin Delivery and Attenuates Washout During Balloon Angioplasty with Hydrogel-Coated Balloons

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Although previous studies have demonstrated that heparin can be delivered to the arterial wall during balloon angioplasty with hydrogel-coated balloons, drug washout over the first hour is rapid. The purpose of this study was to determine whether vascular heating during local heparin delivery with hydrogel-coated, radiofrequency-powered thermal angioplasty balloons would affect immediate drug deposition and the subsequent persistence of heparin within the arterial wall. *To evaluate the effect of heat on heparin deposition,* fluorescein-labeled heparin was delivered in vitro to 13 bovine coronary arteries either at 50°C (n = 3), at 60°C (n = 3) or without heat (n = 7). Heparin deposition was graded on a 1–3 scale as extending into the inner 1/3, the middle 1/3 or outer 1/3 of the arterial wall. *To assess the effect of heat on the intramural persistence of heparin,* ^{3}H-heparin was delivered in vivo to 13 porcine peripheral artery pairs. The balloon:artery ratio was 1.2:1 as guided by intravascular ultrasound. One artery in each pair was heated during heparin delivery to either 50°C (n = 11) or 80°C (n = 2). The contralateral control vessel was not heated. Arteries were harvested at one hour for scintillation counting. In both the in vivo and in vitro studies, balloon inflations were at 6 atm for 2.5 minutes. In all heated vessels thermal energy was applied for 90 secs.

Results: Supplemental heating during local drug delivery significantly increased both the immediate deposition and the persistence of intramurally delivered heparin. In vitro, the heparin deposition score was 2.3 ± 0.5 for heated arteries and 1.3 ± 0.8 for controls (p = < 0.03). In vivo, more heparin was present at one hour in the heated arteries than in the control arteries in 11 of 13 vessel pairs (heated vessels, 58 ± 46 units; non-heated controls, 43 ± 42 units, p = 0.02).

Conclusion: Vascular heating at the time of local heparin delivery with hydrogel-coated balloons increases both the immediate delivery and the persistence of heparin in the arterial wall.

9:30

772-5 Local Intramural Nitroglycerin Delivery Improves Vascular Responses to Balloon Arterial Injury

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Endothelial denuding injury of the arterial wall in vivo is associated with a localized platelet deposition and a vasoconstrictive response, that may be due to loss of endogenous vessel wall EDRF nitric oxide production. Exogenous administration of EDRF in the form of systemic nitroglycerin (NTG) can decrease the injury-related platelet deposition and vasoconstriction. Whether the injured vessel wall EDRF effect can be enhanced by local intramural NTG delivery was studied using a Localmed infusion sleeve. Normal pigs underwent carotid arterial injury by a balloon dilatation catheter placed inside a sleeve with distal micro-perforations designed for intramural drug delivery at the site of angioplasty. In 6 pigs, the left carotid was treated with NTG, while the right carotid was treated with dextrose 5% vehicle. Autologous ^{51}Cr-platelet (PLT) deposition quantified at the site of deep arterial injury by the body of the balloon, and the degree of angiographic vasoconstriction (VC) at the site of endothelial denudation by the tapering ends of the balloon, were assessed before and after NTG or dextrose delivery, and are shown below, (mean ± SEM):

Group	PLT deposition (% control)	VC before (% baseline)	VC after (% baseline)
Dextrose	100	25.7 ± 7.6	28.0 ± 4.2
NTG	59.3 ± 14.0*	26.2 ± 7.2	10.7 ± 8.6†

*P < 0.05 vs dextrose; †P < 0.05 vs VC before

Thus, local administration of NTG directly into the injured arterial wall is effective in decreasing platelet deposition and the vasoconstrictive response after deep arterial injury. This may improve vascular function after balloon injury.

9:45

772-6 Angiopeptin Loaded Stents Inhibit the Neointimal Reaction Induced by Polymer Coated Stents Implanted in Porcine Coronary Arteries

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Poly(organo)phosphazene polymer (PP) coated on metallic coronary stents induce a severe histiolymphocytic and fibromuscular reaction leading to major coronary stenosis 6 weeks after stent implantation in a porcine coronary model. PP coated stents were loaded with angiopeptin (AP) (5 wt %) and stent stenosis was evaluated using quantitative coronary analysis and histopathology. A total of 14 pigs (7 received an AP loaded stent, 7 a non AP loaded stent (NAP) were studied. Minimal luminal stent diameter (MLSD) was measured using a semi-automated edge detection algorithm (Polytron® 1000 Siemens)

Pre stent implantation MLSD:APL:2.5 ± 0.2 mm; NAPL 2.6 ± 0.4 mm (NS). Post stent implantation MLSD:APL:3.0 ± 0.4 mm; NAPL 3.4 ± 0.3 mm (NS). After 6 weeks MLSD was significantly higher in the APL group compared with the NAPL group 2.2 ± 0.6 mm vs 1.7 ± 1.0 mm (p < 0.01).

Histopathology demonstrated a severe histiolymphocytic and fibromuscular reaction in both groups but vessel narrowing was significantly more important in the NAPL group compared with the APL group (87.6 ± 11.5% vs 63.4 ± 18.2%; p < 0.01). These results suggest that local AP delivery using an AP loaded polymer coated stent is able to inhibit the foreign body reaction induced by poly(organo)phosphazene stent coatings.